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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,796	03/13/2000	DOMINIQUE BRASSART	P99.2625	1391

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,796	BRASSART ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-14,16-18 and 21-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14,16-18 and 21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 11-14, 16-19 and 21-26 as amended [paper(s) filed 3/08/2003] are pending and under examination in the instant office action.

Claims 1-10 were canceled by applicants in the Paper No. 10 filed 6/04/2001.

Claims 15 and 20 were canceled by applicants in the Paper No. 20 filed 9/03/2002.

Deposit

The deposit requirement for *Lactobacillus johnsonii* CNCM I-1225 has been met in the Paper No. 10 filed 6/04/2001.

Claim Rejections - 35 USC § 112

New matter

Claims 11-14, 16-19 and 21-26 as amended are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Insertion of limitation "nutritional composition is not a fermented nutritional composition" in the method for treatment or prophylaxis of calcium deficiencies has no support in the as-filed specification. This new limitation is drawn to the exclusion of fermented products from composition with live lactic bacteria in the method for treatment or prophylaxis of calcium deficiencies. This exclusion of fermented products/components as encompassed by the presently amended claims has no support in the as-filed specification.

The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor there are specific examples of the newly limited genus that would show possession of the concept such as exclusion of fermented products/components from the live lactic bacteria-containing compositions in the method for treatment or prophylaxis f calcium deficiencies as presently encompassed by the claimed invention.

The generic disclosure relates to the enteral administration of a nutritional composition that contains lactic bacteria to improve mineral absorption from diets (page 3, line 3-5). The generic disclosure clearly teaches that "the nutritional composition may be fermented" (page 4, line 32) to obtain a sufficient number of lactic bacteria. The specification does not disclose a separation of lactic bacteria from fermented compositions and in vivo administration of lactic bacteria separated from fermented products. The suitable nutritional compositions intended for administration comprise "fermented milk ", "fromage frais", "ripened cheese" (page 6, line 36) that are products fermented by lactic bacteria.

Further, there is no disclosure about exclusion of fermented products as based on particular examples. The particular examples disclose method of making compositions that are suitable for administration wherein these preparations include compositions comprising fermented products or "milk acidified" by *Lactobacillus* and *Bifidobacterium* (page 12, lines 1).

Therefore, the as-filed specification does not teach any intentional exclusion of fermented products from the lactic-bacteria containing composition. The as-filed specification does not point out that the exclusion of fermented products from the lactic-bacteria containing composition would provide any functional effects related to mineral absorption. Although the

live lactic bacteria-containing compositions might be obtained by both fermentation of nutrients with lactic bacteria and by admixing nutrients with live lactic bacteria, the method for treating or preventing calcium deficiencies does not exclude the use of fermented compositions. The critical element in the method for administration for treating calcium deficiency is the use of live lactic bacteria (page 5, lines 23-27) but not the exclusion of fermented products. Moreover, applicants appear to believe that the acidification induced by lactic bacteria might provide some improvements for mineral absorption in intestines (page 5, line 23-27). Acidification is a result of fermentation by lactic bacteria and effects of fermented products that contain acidified products and/or metabolites of lactic bacteria.

Thus, there is no any support for the new concept leading towards the idea of exclusion of fermented products from the live lactic bacteria-containing composition in the method for treating calcium deficiencies. This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept of excluding fermented products from the products that are administered for treating or preventing mineral absorption. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of limitation such as "nutritional composition is not a fermented nutritional composition" in the method for the treatment or prophylaxis of calcium deficiencies is considered to be the insertion of new matter for the above reasons.

Claim Rejections - 35 USC § 102

Applicants are hereby notified that the insertion of new matter into the claims has necessitated the removal of the art rejection over claims under 35 U.S.C. 102(b) as being

anticipated by US 5,494,664. However, removal of new matter will result in the reinstatement of the art rejection(s).

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 11, 12, 16-19, 21, 23 and 24 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sellars R.L. [ref. U-19; "Acidophilus Products". In: "Therapeutic properties of fermented milk". 1991, 81-116] and Yaeshima [ref. IDS-3-AR ; Bulletin of the International Dairy Federation. 1996, No. 313, 36-42] as explained in the prior office action and repeated herein.

Claims are directed to methods for prophylaxis or treatment of calcium deficiencies and for improving absorption of calcium by administering a nutritional composition comprising one or more live bacteria belonging to the genus of *Lactobacillus* to mammal patients at risk of calcium deficiency or in need of increased calcium absorption. Some claims are further drawn to the use of bacteria capable of adhering to intestinal cells. Some claims are further drawn to the use of milk products and/or milk hydrolysates in the nutritional composition in the method of administration.

The reference by Sellars teaches that consumption of "acidophilus" products with sufficient numbers of active viable cells promote mineral absorption (page 100, par. 3, lines 3-6) and that the fermented diary products containing live "lactobacilli" bacteria increase mineral absorption (page 102, par. 2, lines 1-4). Thus, the cited reference clearly teaches and suggests methods for treatment of mineral deficiencies and for improving mineral absorption by

administration of nutritional compositions comprising live "lactobacilli" bacteria of the "acidophilus" products. The "lactobacilli" bacteria of the "acidophilus" products in the reference by Sellars are bacteria belonging to the genus of *Lactobacillus* including *Lactobacillus acidophilus* and others including *Bifidobacterium*, for example: see table see tables I-III at pages 84-86. The reference by Sellars teaches that colonization of gastrointestinal tract (GI) by the "lactobacilli" bacteria of the "acidophilus" products bacteria promote mineral absorption (page 100, par. 3, lines 5-6). The cited reference by Sellars teaches benefits related to absorption of minerals in general but it is lacking particular disclosure about mineral calcium.

However, the reference by Yaeshima [IDS-3-AR] teaches the method for treatment and/or improving absorption of mineral that is calcium by administering to mammals the live cells of *Bifidobacterium* which is representative of "lactobacilli" contained in "acidophilus" products. The reference clearly demonstrates that enteral administration or consumption of the live "lactobacilli" contained in the "acidophilus" bacteria improves calcium absorption and increases bone strength. For example: see page 41, col. 1-2; Fig. 13; page 41, col. 2, lines 3-5. The reference by Yaeshima also teaches that the representatives of the whole group of the lactic bacteria including both "bifidobacteria" and "lactobacilli" are typical examples of beneficial bacteria residing in the intestines that contribute to digestion and absorption (page 36, col. 1, par. 1-2).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use live lactic bacteria of the genus *Lactobacillus* for administration to mammals at risk of calcium deficiency or in need of increased calcium absorption with a reasonable expectation of success in treating calcium deficiency and/or

improving calcium absorption because consumption of live lactic bacteria including both *Lactobacillus* and *Bifidobacterium* promotes and increases mineral absorption and because the representatives of the whole group of lactic bacteria have demonstrated to increase calcium absorption. One of skill in the art would have been motivated to administer live lactic bacteria to mammals having mineral deficiency including calcium deficiency or to mammals requiring increase mineral absorption including calcium absorption for the expected benefits in treating mineral deficiency including calcium deficiency and/or improving mineral absorption including calcium absorption. One of skill in the art is free to select beneficial bacteria from the whole group of lactic bacteria since the whole group of lactic bacteria is regarded as being beneficial for mineral absorption including calcium absorption. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary. Further, it is considered to be within the skills of an ordinary practitioner in the field to use the additional components including milk protein hydrolysates or prebiotic fibers in the nutritional compositions intended for treatment or prophylaxis of mineral deficiencies including calcium deficiencies or for improving absorption of calcium from diets depending on patient age, life style and/or general state of health. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Claims 11-14, 16-19 and 21-26 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sellars R.L. and Yaeshima as applied to claims 11, 12, 16-19, 21, 23 and 24 above, and further in view of US 5,494,664 and US 5,578,302 as explained in the prior office action and repeated herein.

Claims 11, 12, 16-21, 23 and 24 as explained above. Some claims are further drawn to the use of bacteria capable of adhering to intestinal cells or particular strain CNCM I-1225 belonging to *Lactobacillus johnsonii (*priory identified as *acidophilus).* Some claims are further drawn to the use of bacteria in amounts 10^7 to 10^{11} CFU/ml in the method of administration of the nutritional composition.

Both cited references by Sellars and by Yaeshima teach that the benefits related to mineral absorption including calcium absorption are the result of administration of lactic bacteria. But they are lacking particular disclosure related to the use of a particular lactic bacterium which is strain CNCM I-1225 *Lactobacillus johnsonii.*

However, the cited US 5,494,664 and US 5,578,302 discloses the therapeutic use of the particular strain CNCM I-1225 *Lactobacillus johnsonii (*previously identified as *acidophilus)* which is capable to colonize GI and to adhere to intestinal cells and which promotes health benefits in mammals. The therapeutic applications in the cited patents are based on GI colonization by lactic bacteria and, in particular, by bacterial cells of the strain CNCM I-1225 *Lactobacillus johnsonii.*

The cited reference by Sellars teaches that the colonization of gastrointestinal tract by the lactic bacteria promotes and increases mineral absorption. The cited reference by Yaeshima teaches that the residence or the establishment of lactic bacteria in the intestines of mammals promotes health benefits and increases calcium absorption and bone strength. But the cited references by Sellars and by Yaeshima are silent about the particular amounts that are required for GI colonization.

However, the cited US 5,494,664 teaches the particular amounts of live bacterial cells including the strain CNCM I-1225 such as 10^7 to 10^{11} CFU/ml which provide for GI colonization and for bacterial residence in intestines (col. 4, lines 66-67, col. 3, lines 1-3 and 22-25). The cited patent US 5,494,664 also teaches that traditional yogurt, which is one of the

"acidophilus" product of the reference by Sellars, is believed to provide for the similar amounts of lactic bacteria (col. 3, lines 35-37) that are sufficient to establish residence or colonize GI.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use live bacteria of the strain CNCM I-1225, which is *Lactobacillus johnsonii (*priory identified as *acidophilus),* in the method of administering to mammals in needs of mineral absorption including calcium absorption with a reasonable expectation of success in treating mineral deficiencies including calcium deficiency in mammals and/or improving absorption of minerals including calcium in mammals because bacteria from the same group of lactic bacteria have been taught and/or suggested for the same purpose of improving mineral absorption including calcium absorption as adequately demonstrated by these cited references by Sellars and by Yaeshima. One having ordinary skill in the art would have been motivated to use the strain CNCM I-1225 because this strain has been taught as capable to colonize GI and the colonization of GI promotes mineral absorption including calcium absorption. One having ordinary skill in the art would have been motivated to use about 10^7 to 10^{11} CFU/ml amounts of lactic bacteria in the compositions in the methods in treating mineral deficiencies including calcium deficiency in mammals and/or improving absorption of minerals including calcium from diets because the prior art teaches that these amounts of lactic bacteria are sufficient for GI colonization and because the GI colonization promotes mineral absorption including calcium absorption as adequately demonstrated by the cited prior art. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Response to Arguments

Applicants' arguments filed 3/08/2004 have been fully considered but they are not persuasive.

With regard to the reference by Sellars applicants argue that it only recognizes the beneficial effects of lactic bacteria fermented products as related to mineral absoption (response page 6). Upon review of the reference it is not find true because Sellars points out that the colonization of GI tract by lactic bacteria promotes rate of mineral absorption (page 100, par. 3,lines 5-6). Thus, Sellars recognizes the lactic bacteria as beneficial factor and the fermented products as a source of live bacteria capable to colonize GI tract. The fact that Sellars also teaches beneficial effects of lactic acid does not teaches away because lactic acid is a metabolite of lactic bacteria that are live, active, capable to grow and to colonize GI tract. Moreover, applicants also consider lactic acid as a factor in GI acidification that leads to improvement in mineral absorption (page 5, lines 23-28).

As related to the teaching of the reference by Yaeshima applicants argue that it teaches only the use of *Bifidobacterium* in the method for improving calcium absorption and, thus, one of skill in the art would not have been motivated to substitute lactobacilli for bifidobacteria because these bacteria belong to "completely different phyla" (response page 7). However, taxonomic assignment of bacteria to different genera or "phyla" is based on a complex of artificially selected features that are not necessarily functional as related to the *in vivo* methods of treatment. The fact that both bifidobacteria and lactobacilli are beneficial microflora of GI and that both bifidobacteria and lactobacilli are capable to colonize GI is an evidence of their functional similarity that provide for the effects related to gastrointestinal mineral absorption improvement including calcium absoption improvement. Moreover, the reference by Yaeshima recognizes functional similarity of bifidobacteria and lactobacilli for digestion and absorption of nutrients (page 36, col. 2, line 1).

The cited patents '664 and '302 are relied upon to demonstrate known therapeutic value of the presently claimed strain CNCM I-1225 *Lactobacillus johnsonii (*previously identified as *acidophilus).* This strain is known to be capable to colonize GI, to adhere to intestinal cells and to promote health benefits in mammals. The therapeutic applications of live lactic bacteria are based on GI colonization by lactic bacteria and, the particular strain CNCM I-1225 is known to function accordingly. The reference by Sellars and by Yaeshima clearly teach that the GI colonization by live lactic bacteria promotes the mineral absorption. Thus, the invention as a whole would have been obvious under 35 U.S.C. 103.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Vera Afremova

AU 1651

May 18, 2004

V. Afremova

VERA AFREMOVA

PATENT EXAMINER